

Rejections under 35 U.S.C. §§ 101 and 112, First Paragraph

The Examiner maintains rejection of claims 25-79 under 35 U.S.C. § 101 as allegedly not being "supported by either a specific and substantial asserted utility or a well-established utility." In particular, the Examiner alleges that "[t]he instant application does not disclose the biological role of this protein or its significance." *See*, Paper No. 10, Pages 3-4.

Applicants again respectfully disagree and traverse this rejection.

A rejection under 35 U.S.C. § 101 is improper when a person of ordinary skill in the art would find credible disclosed features or characteristics of the invention, or statements made by the applicant in the written description of the invention. *See*, M.P.E.P. §§ 2107.01(II), (III) at 2100-[29-31] (Rev. 1, Feb. 2000). In addition, an applicant need only make *one* credible assertion of utility for the claimed invention to satisfy 35 U.S.C. § 101. *See, e.g., Raytheon v. Roper*, 724 F.2d 951, 958, 220 U.S.P.Q. 592, 598 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 835 (1984) ("When a properly claimed invention meets at least one stated objective, utility under 35 U.S.C. § 101 is clearly shown."). *See*, M.P.E.P. at 2100-29. Finding a lack of utility is also improper if a person of ordinary skill in the art would know of a use for the claimed invention at the time the application was filed. M.P.E.P. § 2107.01(II)(B) at 2100-[29-30].

Moreover, the burden is on the Examiner to establish why it is more likely than not that one of ordinary skill in the art would doubt (*i.e.*, "question") the truth of the statement of utility. M.P.E.P. § 2107.01(II)(A) at 2100-[31-32]. Thus, the Examiner must provide evidence sufficient to show that the statement of asserted utility would be considered "false" by a person of ordinary skill in the art. *Id.* The Examiner must also present countervailing facts and reasoning sufficient to establish that a person of ordinary skill would not believe the applicants' assertion of utility. *See id.*; *see also, In re Brana*, 51

F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995). For the reasons set forth below, the Examiner has not met the burden that is necessary to establish and maintain a rejection for lack of utility under 35 U.S.C. § 101.

As previously described by Applicants (*see* Paper No. 12, pages 4-5), and contrary to the Examiner's comments, the specification contains statements that clearly and fully describe the function and usefulness of Human Cytokine Polypeptide of the present invention. For example, the specification, at page 3, lines 5-8, teaches that polypeptides of the present invention may stimulate cell proliferation and/or differentiation and may be used to treat, for example, restenosis and/or inflammation. Also, the specification, for example at page 37, lines 7-13, teaches that polypeptides of the invention have further related uses, for example, in the detection of neoplasia, a disorder characterized by abnormal cellular proliferation. Moreover, the specification, for example at page 37, line 15 to page 38, line 13, teaches exemplary methods by which such a disorder may be detected using polypeptides of the invention. Applicants repeat their assertion, that such characterization of the invention is sufficient to constitute a showing of utility as required under 35 U.S.C. § 101.

In support of utilities asserted in the specification as filed, Applicants previously submitted the teachings of Graf et al. and Oelgeschläger et al. *See* Paper No. 12, pages 5-6. These references teach that Human Cytokine Polypeptide of the present invention shares 100% sequence identity with the human homologue of the *twisted gastrulation* protein from *Drosophila melanogaster*; that in the fruitfly this polypeptide is a secreted protein which functions by direct interaction with Bone Morphogenetic Proteins (BMPs); and that this polypeptide functions by a similar mechanism in vertebrates and in flies. From this evidence, one skilled in the art would appreciate that the pending claims of the

present invention are indeed supported by specific and substantial utilities, which are entirely credible in light of the state of knowledge in the art.

However, the Examiner finds Applicants' assertions of utility to be unconvincing.

In dismissing Applicants' arguments, the Examiner states:

[t]he particular cytokine claimed has no utility till Applicants disclose what tissue or cell types the cytokine acts upon and the effects the cytokine has on the cells. For example if an antibody was claimed, it would not be disputed that the antibody was an antibody, but not knowing the antigen to which the antibody specifically binds, would make the claimed antibody not useful. Furthermore, the employment of the polypeptide of the instant invention, in the example cited by Applicants (in detection of neoplasia) is not a substantial or specific utility, because the cytokine protein has not shown to be associated with a disease or condition in any tissue.

Applicants respectfully disagree and point out that polypeptides of the invention regulate cellular proliferation and/or differentiation and may therefore be used, for example, in the detection of neoplasia. Applicants further point out that such a use does constitute a specific utility, in that not every polypeptide serves to regulate cellular proliferation and/or differentiation; a substantial utility, in that detection of disorders such as neoplasia is of vital importance to patients and physicians; and a credible utility, in that all evidence of record indicates, and none contradicts, that it was possible to successfully detect, diagnose and even treat such conditions at the priority date of the present invention. The Examiner contends that the patentability of the present invention, based on this utility, is dependent on disclosure of the details of how or why the invention works. Applicants respectfully but emphatically note that this assertion is contrary to well established law. The Federal Circuit has recently stated with respect to the rejection of claims for lack of utility that:

"It is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works." Newman v. Quigg, 877 F.2d 1575, 1581, 11 U.S.P.Q.2D (BNA) 1340, 1345 (Fed. Cir. 1989); see also

Fromson v. Advance Offset Plate, Inc., 720 F.2d 1565, 1570, 219 U.S.P.Q. (BNA) 1137, 1140 (Fed. Cir. 1983) ("It is axiomatic that an inventor need not comprehend the scientific principles on which the practical effectiveness of his invention rests."). Furthermore, statements that a physiological phenomenon was observed are not inherently suspect simply because the underlying basis for the observation cannot be predicted or explained.

In re Cortright, 49 U.S.P.Q.2d 1464, 1466 (Fed. Cir. 1999). Likewise, according to the axiom of patent law, the utilities asserted for the Human Cytokine Polypeptide do not depend on identification of any receptor or cofactor necessary for its biological activity. Rather, the issue is whether an asserted utility is true.

The Examiner further claims, that "contrary to Applicants arguments, as set forth at pages 3-5 of the previous Office action (Paper No. 10, 9/7/00), the instant situation is directly analogous to that which was addressed in *Brenner v. Manson*, 148 U.S.P.Q. 689 (*Sus. Ct*, 1966)... ."

Applicants respectfully disagree and point out that at issue in *Brenner v. Manson* was whether a process was patentable, where the product of said process had no demonstrable utility. In *Brenner v. Manson* the "respondent himself recognized that the presumption that adjacent homologues have the same utility has been challenged in the steroid field because of 'a greater known unpredictability of compounds in that field.'" In stark contrast, the present case involves a Human Cytokine polypeptide which has been identified as a human homolog of *twisted gastrulation*, a protein which binds BMPs thereby regulating cellular proliferation and differentiation. The use of homology analysis has been used successfully in the identification of a vast array of polypeptide molecules and has achieved wide-ranging acceptance by those of skill in the art of molecular biology. In support of homology analysis in the assignment of protein function, Doerks et al. (Paper No. 13, reference R cited by the Examiner) teach that "[c]omputer analysis of genome

sequences is currently one of the essential steps for obtaining functional and structural information about the respective gene products." See Doerks et al., Trends in Genetics. June 1998, Vol. 14, No. 6: pages 248-250, at page 248, column 1, paragraph 1. Therefore, in contrast to the situation in *Brenner v. Manson*, the present invention describes a Human Cytokine Polypeptide whose function has been characterized using routine techniques and whose asserted utility would be entirely credible to one of skill in the art.

In an attempt to undermine the value of computer based analysis of protein function the Examiner alleges that:

it is commonly known in the art that sequence-to-function methods of assigning protein function are prone to errors. (Doerks et al. 1998). These errors can be due to sequence similarity of the query region to a region of the alleged similar protein that is not the active site, as well as homologs that did not have the same catalytic activity because active site residues of the characterized family were not conserved (Doerks et al., page 248, column 3, fourth and fifth paragraphs). Inaccurate use of sequence-to-function methods have led to significant function-annotation errors in the sequence databases (Doerks et al. Page 250, column 1, third paragraph).

Applicants respectfully dispute the relevance of the Examiner's argument and submit that even should this allegation prove correct, the Examiner has provided no evidence or logical argument to suggest that a sequence-to-function analysis has led to an error in the present case. The same reference cited by the Examiner also teaches "[c]omputer analysis of genome sequences is currently one of the essential steps for obtaining functional and structural information about the respective gene products" (page 248, column 1, paragraph 1); and "[a]nnotation with the right level of precision helps in future projects. In summary, we were able to provide some functional annotation for more than 700 of about 1300 proteins" (page 250, column 1, paragraph 2). Therefore, Applicants contend that the evidence submitted does not support the Examiner's position that computer based analysis of protein function is inherently unbelievable and/or unreliable. In other words, the teaching of Doerks et al. is entirely consistent with the

asserted function of the Human Cytokine Polypeptide being more likely than not true. Inspection reveals that the mature polypeptide of the present invention shares approximately 90% sequence identity with the mature *Xenopus* homologue of *twisted gastrulation*, as taught by Oelgeschläger et al. (Nature, 405: pp 757-763. (2000)), while the N-terminal predicted BMP-binding domains of these homologues share approximately 95% sequence identity. Furthermore, this reference teaches that the *Xenopus* homologue of *twisted gastrulation* binds the same signaling molecules, and performs a similar function as does *twisted gastrulation* in *Drosophila*. In light of this evidence, one of skill in the art would find that Applicants' initial assertion, that the Human Cytokine Polypeptide of the present invention may regulate cellular proliferation and differentiation and may therefore be useful, for example, in the detection of neoplasia, is indeed credible.

Other than reiteration of conclusory statements that the invention lacks utility, the Examiner has presented no arguments as to why this asserted utility is not credible. In arguing that Applicants' asserted utility is not credible, the Examiner has not attacked (a) the logic underlying the assertion as seriously flawed or (b) the facts upon which the assertion is based as inconsistent with the logic underlying the assertion. See, Revised Interim Utility Guidelines Training Materials, p. 5. In the instant rejection, the Examiner has set forth no arguments as to why Applicants' logic (that Human Cytokine Polypeptide of the present invention has the activity of modulating cell proliferation and/or differentiation) is flawed or that the facts upon which the logic is based on, are inconsistent with the underlying assertion. Thus, the Examiner has failed to make even a *prima facie* showing that Applicants' asserted utility is not credible.

Once more, Applicants respectfully submit that the Human Cytokine Polypeptide of the invention (such as, for example, the polypeptide shown as SEQ ID NO:2), has an immediate and specific utility. Such polypeptide may regulate cell proliferation and/or

differentiation and therefore, polypeptides of the instant invention, or agonists or antagonists thereof, may be used to treat and/or prevent and/or detect disorders of cell differentiation and/or proliferation such as, for example, neoplasia. Thus, polypeptides of the invention are supported by an immediate utility that is both specific and substantial.

In summary, these asserted utilities for Human Cytokine Polypeptide are specific (not every protein modulates cell proliferation and/or differentiation) and substantial ("the general rule [is] that the treatments of specific diseases or conditions meet the criteria of 35 U.S.C. § 101." (Revised Interim Utility Guidelines Training Materials, p. 6)). In addition, these utilities are credible and evidentiary support for this credibility has been provided (*See* Paper No. 12). The Examiner has failed, however, to provide any countervailing statements as to why these particular utilities are not specific, substantial and credible.

In regard to these asserted therapeutic activities, Applicants note that there is no need to prove that a correlation exists between a particular activity and an asserted therapeutic use of a compound as a matter of statistical certainty or provide actual evidence of success in treating humans where such a utility is asserted. M.P.E.P. § 2107.02 (I) at 2100-[33-34]. All that is required of Applicants is that there be a reasonable correlation between the biological activity and the asserted utility. *See, Nelson v. Bowler*, 626 F.2d 853, 857 (C.C.P.A. 1980). Moreover, "[u]sefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development. The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." *In re Brana*, 51 F.3d 1560, 1568 (Fed. Cir. 1995) (emphasis added).

Even assuming, *arguendo*, the Examiner has established a *prima facie* showing that the claimed invention lacks utility, Applicants respectfully submit that they have

rebutted the Examiner's showing by proffering sufficient evidence to lead one skilled in the art to conclude that the asserted utilities are more likely than not true. Applicants have directed the Examiner to the specification where clear and specific assertions are made of Human Cytokine polypeptide biological and therapeutic activity.

In view of the above, Applicants submit that the asserted utilities of the invention meet the statutory requirement set forth in 35 U.S.C. § 101. The Examiner has failed to establish and maintain grounds as to why a rejection for lack of utility is proper. Accordingly, Applicants respectfully request that the rejection of claims 25-79 under 35 U.S.C. § 101 be withdrawn.

The Examiner has also rejected claims 25-79 under 35 U.S.C. § 112, first paragraph, "since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention".

Applicants respectfully disagree and traverse this rejection.

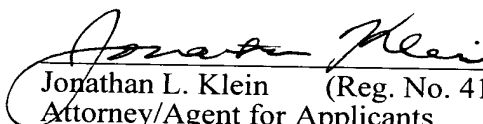
As detailed above, the asserted utilities of the invention meet the statutory requirement set forth in 35 U.S.C. § 101 and, armed with the specification of the instant invention, one skilled in the art clearly would know how to use the claimed invention. Accordingly, Applicants respectfully request that the rejection of claims 25-79 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Conclusion

Applicants respectfully request consideration and entry of the foregoing remarks into the file. Applicants believe that no fee is due in connection herewith; however, should the Patent Office determine otherwise, please charge the required fee to Human Genome Sciences, Inc., Deposit Account No. 08-3425.

Respectfully submitted,

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Enclosures

JKE/BM